National Institute for Health and Care Excellence

Final

Subarachnoid haemorrhage caused by a ruptured aneurysm: diagnosis and management

[G] Evidence review for detecting hydrocephalus

NICE guideline NG228

Methods, evidence and recommendations

November 2022

Final

National Institute for Health and Care Excellence

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The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and, where appropriate, their carer or guardian.

Local commissioners and providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

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Evidence review underpinning recommendation 1.3.3 in the NICE guideline.

1.1 Review question: What is the diagnostic accuracy of investigations for detecting hydrocephalus for the person with aSAH and signs of neurological deterioration?

1.2 Introduction

Hydrocephalus is diagnosed when a patient presents with symptoms and signs of raised intracranial pressure and axial imaging of the brain shows enlargement of the ventricular system (the fluid filled chambers within the brain). Ventricular dimensions can be assessed equally effectively on CT and MRI but imaging evidence of ventricular enlargement alone is insufficient to diagnose hydrocephalus, as enlarged ventricles may be long-standing in some people.

Up to a third of patients with aneurysmal SAH develop acute hydrocephalus within a few days of presentation, and the dimensions of the ventricular system are generally assessed on a non-contrast CT scan, and correlated with previous CT imaging (if available) and the patient's clinical status.

The pathogenesis of hydrocephalus in people with aSAH is complex, but thought to be due to obstruction of CSF flow, or reduction of CSF reabsorption. The probability of developing hydrocephalus is increased when SAH is associated with: worse clinical grade, large volume of blood in the basal cisterns, intra-ventricular haemorrhage, posterior circulation aneurysm, or systemic hypertension.

Up to half of patients with a reduced GCS score due to acute hydrocephalus will improve without surgical management but comatose patients require prompt ventricular drainage.

A proportion of patients with acute hydrocephalus will go on to develop chronic (shunt-dependent) hydrocephalus and may require longer term CSF diversion, usually with a ventriculo-peritoneal shunt.

This evidence review was carried out to assess the diagnostic accuracy of MR imaging for the detection of hydrocephalus in people with aneurysmal SAH, relative to the reference standard of non-contrast CT.

1.3 PICO table

For full details see the review protocol in Appendix A:.

Table 1: PICO characteristics of review question

Population	Inclusion: Adults (16 and older) with a confirmed subarachnoid haemorrhage caused by a ruptured aneurysm and with signs of neurological deterioration. Exclusion: • Adults with subarachnoid haemorrhage caused by head injury, ischaemic stroke or an arteriovenous malformation. • Children and young people aged 15 years and younger.
Target condition	Acute hydrocephalus in people with aneurysmal subarachnoid haemorrhage
Index test(s) (comparator(s))	MRI

Reference standard(s)	Non-Contrast CT
Statistical measures [or] Outcomes	Statistical measure to detect hydrocephalus: • Sensitivity • Specificity
Study design	• Cross-sectional studies • Cohort studies • Systematic reviews of observational cohort studies will be included

1.4 Clinical evidence

1.4.1 Included studies

No relevant diagnostic accuracy studies of MR imaging to detect hydrocephalus in people with aSAH were identified.

See also the study selection flow chart in Appendix C:.

1.4.2 Excluded studies

See the excluded studies list in Appendix H:.

1.4.3 Summary of clinical studies included in the evidence review

No evidence was identified for this review.

1.4.4 Quality assessment of clinical studies included in the evidence review

No evidence was identified for this review.

1.5 Economic evidence

1.5.1 Included studies

No health economic studies were included.

1.5.2 Excluded studies

No relevant health economic studies were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in Appendix F:.

1.5.3 Unit costs

Relevant unit costs are provided in Table 2 to aid consideration of cost effectiveness.

Table 2: UK costs of diagnostic tests for aneurysmal subarachnoid haemorrhage

Diagnostic test description	Cost
Computerised Tomography Scan of One Area, without Contrast, 19 years and over [NHS Reference cost code: RD20A]	£78
Magnetic Resonance Imaging Scan of One Area, without Contrast, 19 years and over [NHS Reference cost code: RD01A]	£121

Source: NHS Reference Costs 2018/19[6]

1.6 Evidence statements

1.6.1 Clinical evidence statements

No evidence was identified for this review

1.6.2 Health economic evidence statements

No relevant economic evaluations were identified.

1.7 The committee's discussion of the evidence

1.7.1 Interpreting the evidence

1.7.1.1 The diagnostic measures that matter most

The objective of this review was to assess the diagnostic accuracy of MR imaging for detecting hydrocephalus, relative to a reference standard of CT head scan. Sensitivity and specificity of MRI imaging to detect hydrocephalus were the outcomes for this review.

1.7.1.2 The quality of the evidence

No evidence was identified for this review. The committee made a consensus recommendation reflecting standard current practice on the use of comparative CT head scans to confirm a diagnosis of hydrocephalus.

1.7.1.3 Benefits and harms

The committee agreed that hydrocephalus is suspected on the basis of symptoms and signs of raised intracranial pressure, such as altered level of consciousness or neurological deterioration. In current practice a diagnosis of hydrocephalus is confirmed by enlargement of the ventricular system on a CT head scan in comparison with previous CT head scans or other brain imaging. The main benefit of detecting hydrocephalus as the cause of acute neurological deterioration is to enable diversion or drainage of CSF, to reduce the pressure on the brain, and relieve symptoms (such as headache, nausea, impaired vision, and reduced mobility).

Acute hydrocephalus:

Acute neurological deterioration in a person with aSAH is a medical emergency and needs rapid assessment and management. In current practice, patients with acute neurological deterioration are investigated with a CT head scan to exclude other causes of deterioration (such as further bleeding), and allow comparison with previous CT head scans or other imaging to detect enlargement of the ventricular system. From their clinical experience the committee agreed that acute hydrocephalus is common in people with aSAH and timely investigation and diagnosis are important to facilitate treatment and avoid disability and death. The committee highlighted that clinical judgment should be used to determine if the interval between comparative CT scans is sufficient to demonstrate ventricular enlargement and confirm a diagnosis of acute hydrocephalus. The committee made a consensus recommendation to diagnose acute hydrocephalus using a comparative review of current and previous CT or other brain imaging.

Chronic hydrocephalus:

From their experience the committee noted that chronic hydrocephalus is uncommon and typically presents several weeks or months after aSAH with reduced consciousness, gait disturbance or other neurological symptoms. The committee acknowledged that in current practice a person with suspected chronic hydrocephalus late after aSAH will generally be investigated with a CT brain scan to assess ventricular dimensions. The committee agreed that a diagnosis of chronic hydrocephalus should take account of the person's clinical condition and the radiological findings, including a comparative review of a current CT head scan and previous CT or other brain imaging. As such, the committee made a second consensus recommendation to diagnose chronic hydrocephalus taking account of the person's symptoms and signs and radiological evidence using a comparative review of current and previous CT or other brain imaging.

The committee discussed the potential role of MR imaging in the investigation of people with aSAH and suspected hydrocephalus. The committee agreed a CT scan is safer than MR imaging in a person with signs of neurological deterioration. MR scans take longer and the patient is enclosed within the scanner, which limits access to an intubated patient or in an emergency situation. The committee considered MR imaging to be a difficult procedure to undertake in a person who is unwell and CT is the most efficient diagnostic imaging modality for suspected hydrocephalus in people with aSAH and acute neurological deterioration. For these reasons the committee agreed to make a strong recommendation to diagnose hydrocephalus with CT head scan and agreed that a research recommendation for the use of MR imaging in the diagnosis of hydrocephalus was unwarranted.

In a separate review of the management of acute and chronic hydrocephalus, the committee made consensus recommendations to consider drainage or diversion of cerebrospinal fluid for people with neurological deterioration caused by hydrocephalus.

1.7.2 Cost effectiveness and resource use

No published economic evidence was identified for this review. Unit costs were presented to the committee for consideration of cost effectiveness.

The committee considered a non-contrast CT scan to be the reference standard and hence most accurate imaging modality for detecting hydrocephalus. Given that a non-contrast CT scan is less costly than an MRI scan, the committee considered a non-contrast CT scan to be the most cost-effective imaging modality for detecting hydrocephalus. Moreover, in most patients a CT scan can be compared directly with the diagnostic CT scan recorded on initial presentation with suspected subarachnoid haemorrhage.

The committee noted that this is current practice and so do not expect the recommendations to have a substantial resource impact for England.

1.7.3 Other factors the committee took into account

The committee also considered that CT imaging may be more readily available than MRI imaging in an acute setting in the NHS in England.

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Appendices

Appendix A: Review protocols

Table 3: Review protocol: Detecting hydrocephalus

Field	Content
PROSPERO registration number	CRD42020177951
Review title	What is the diagnostic accuracy of investigations for detecting hydrocephalus for the person with aSAH and signs of neurological deterioration?
Review question	What is the diagnostic accuracy of investigations for detecting hydrocephalus for the person with aSAH and signs of neurological deterioration?
Objective	To determine which investigation is the most accurate to detect hydrocephalus in a person with aSAH and signs of neurological deterioration.
Searches	The following databases (from inception) will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE Searches will be restricted by: • English language studies • Human studies The full search strategies will be published in the final review.
Condition or domain being studied	Acute hydrocephalus in people with aneurysmal subarachnoid haemorrhage
Population	Inclusion: Adults (16 and older) with a confirmed subarachnoid haemorrhage caused by a ruptured aneurysm and with signs of neurological deterioration. Exclusion: • Adults with subarachnoid haemorrhage caused by head injury, ischaemic stroke or an arteriovenous malformation. • Children and young people aged 15 years and younger.
Index test	• MRI
Reference standard	• Non-contrast CT
Types of study to be included	• Cross-sectional studies • Cohort studies

	• Systematic reviews of observational cohort studies will be included.
Other exclusion criteria	Exclusions: • Studies that do not report sensitivity and specificity, or insufficient data to derive these values. • Non English language studies.
Context	Hydrocephalus is a serious complication of aSAH. In clinical practice, a person with aSAH who is deteriorating neurologically will undergo investigatory tests to determine the cause of deterioration. In current practice the first line investigation will be a non-contrast CT head. The diagnosis accuracy of tests to hydrocephalus will allow for appropriate investigations of the deteriorating person.
Primary outcomes (critical outcomes)	Statistical measure to detect hydrocephalus: • Sensitivity • Specificity
Secondary outcomes (important outcomes)	Statistical measure to detect hydrocephalus: • Positive Predictive Value (PPV) • Negative Predictive Value (NPV) • Receiver Operating Characteristic (ROC) curve or area under curve
Data extraction (selection and coding)	EndNote will be used for reference management, sifting, citations and bibliographies. All references identified by the searches and from other sources will be screened for inclusion. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4).
Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. Diagnostic test accuracy studies risk of bias will be assessed using QUADAS-2. 10% of all evidence reviews are quality assured by a senior research fellow. This includes checking: • papers were included /excluded appropriately • a sample of the data extractions • correct methods are used to synthesise data • a sample of the risk of bias assessments Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.

<table>
<tr><td>Strategy for data synthesis</td><td colspan="3">Aggregate data on diagnostic accuracy of investigations will be collected and synthesized in a quantitative data analysis. Endnote will be used for bibliography, citations, sifting and reference management. WinBUGS will be used for meta-analysis of diagnostic accuracy studies if included studies are sufficiently homogeneous. Where mete-analysis cannot be performed results will be reported in full on a per-study basis and summary values will be presented as median values. A summary of result will be presented following a modified GRADE approach. Data synthesis will be completed by two reviewers, with any disagreements resolved by discussion, or if necessary a third independent reviewer.</td></tr>
<tr><td>Analysis of sub-groups</td><td colspan="3">None</td></tr>
<tr><td rowspan="8">Type and method of review</td><td>☐</td><td colspan="2">Intervention</td></tr>
<tr><td>☒</td><td colspan="2">Diagnostic</td></tr>
<tr><td>☐</td><td colspan="2">Prognostic</td></tr>
<tr><td>☐</td><td colspan="2">Qualitative</td></tr>
<tr><td>☐</td><td colspan="2">Epidemiologic</td></tr>
<tr><td>☐</td><td colspan="2">Service Delivery</td></tr>
<tr><td>☐</td><td colspan="2">Other (please specify)</td></tr>
<tr><td></td><td colspan="2"></td></tr>
<tr><td>Language</td><td colspan="3">English</td></tr>
<tr><td>Country</td><td colspan="3">England</td></tr>
<tr><td>Anticipated or actual start date</td><td colspan="3"></td></tr>
<tr><td>Anticipated completion date</td><td colspan="3">3 February 2021</td></tr>
<tr><td rowspan="8">Stage of review at time of this submission</td><td>Review stage</td><td>Started</td><td>Completed</td></tr>
<tr><td>Preliminary searches</td><td>☑</td><td>☑</td></tr>
<tr><td>Piloting of the study selection process</td><td>☑</td><td>☑</td></tr>
<tr><td>Formal screening of search results against eligibility criteria</td><td>☑</td><td>☑</td></tr>
<tr><td>Data extraction</td><td>☑</td><td>☑</td></tr>
<tr><td>Risk of bias (quality) assessment</td><td>☑</td><td>☑</td></tr>
<tr><td>Data analysis</td><td>☑</td><td>☑</td></tr>
<tr><td></td><td colspan="2"></td></tr>
<tr><td>Named contact</td><td colspan="3">5a. Named contact
National Guideline Centre</td></tr>
</table>

	5b Named contact e-mail SAH@nice.org.uk 5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and the National Guideline Centre
Review team members	From the National Guideline Centre: • Ms Gill Ritchie • Mr Ben Mayer • Mr Audrius Stonkus • Mr Vimal Bedia • Ms Emma Cowles • Ms Jill Cobb • Ms Amelia Unsworth
Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.
Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website.
Other registration details	
Reference/URL for published protocol	
Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts

	• issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.	
Keywords	Subarachnoid haemorrhage, hydrocephalus, computed tomography, MRI	
Details of existing review of same topic by same authors	None	
Current review status	☐	Ongoing
	☐	Completed but not published
	☐	Completed and published
	☐	Completed, published and being updated
	☐	Discontinued
Additional information		
Details of final publication	www.nice.org.uk	

Table 4: Health economic review protocol

Review question	All questions where health economic evidence applicable
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2003, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual.[5] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will decide based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded based on applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable). • OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden).

	• OECD countries with predominantly private health insurance systems (for example, Switzerland). • Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations. *Health economic study type:* • Cost–utility analysis (most applicable). • Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 2003 or later but that depend on unit costs and resource data entirely or predominantly from before 2003 will be rated as 'Not applicable'. • Studies published before 2003 will be excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the health economic analysis:* • The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix B: Literature search strategies

This literature search strategy was used for the following review;

- What is the diagnostic accuracy of investigations for detecting hydrocephalus for the person with aSAH and signs of neurological deterioration?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual[5]

For more information, please see the Methods Report published as part of the accompanying documents for this guideline.

B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 5: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 24 June 2020	Exclusions Randomised controlled trials Systematic review studies Observational studies Diagnostic tests studies
Embase (OVID)	1974 – 24 June 2020	Exclusions

Database	Dates searched	Search filter used
		Randomised controlled trials Systematic review studies Observational studies Diagnostic tests studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2020 Issue 6 of 12 CENTRAL to 2020 Issue 6 of 12	None

Medline (Ovid) search terms

1.	exp Subarachnoid Hemorrhage/
2.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) adj3 (hemorrhag* or haemorrhag* or bleed* or blood*)).ti,ab.
3.	(SAH or aSAH).ti,ab.
4.	exp Intracranial Aneurysm/
5.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial or brain) adj3 (aneurysm* or aneurism* or hematoma* or haematoma*)).ti,ab.
6.	or/1-5
7.	letter/
8.	editorial/
9.	news/
10.	exp historical article/
11.	Anecdotes as Topic/
12.	comment/
13.	case report/
14.	(letter or comment*).ti.
15.	or/7-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animals/ not humans/
19.	exp Animals, Laboratory/
20.	exp Animal Experimentation/
21.	exp Models, Animal/
22.	exp Rodentia/
23.	(rat or rats or mouse or mice).ti.
24.	or/17-23
25.	6 not 24
26.	(exp child/ or exp pediatrics/ or exp infant/) not (exp adolescent/ or exp adult/ or exp middle age/ or exp aged/)
27.	25 not 26
28.	limit 27 to English language
29.	exp "Sensitivity and Specificity"/
30.	(sensitivity or specificity).ti,ab.
31.	((pre test or pretest or post test) adj probability).ti,ab.
32.	(predictive value* or PPV or NPV).ti,ab.
33.	likelihood ratio*.ti,ab.
34.	likelihood function/

35.	((area under adj4 curve) or AUC).ti,ab.
36.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
37.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
38.	gold standard.ab.
39.	or/29-38
40.	Epidemiologic studies/
41.	Observational study/
42.	exp Cohort studies/
43.	(cohort adj (study or studies or analys* or data)).ti,ab.
44.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
45.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
46.	Controlled Before-After Studies/
47.	Historically Controlled Study/
48.	Interrupted Time Series Analysis/
49.	(before adj2 after adj2 (study or studies or data)).ti,ab.
50.	exp case control study/
51.	case control*.ti,ab.
52.	Cross-sectional studies/
53.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
54.	or/40-53
55.	Meta-Analysis/
56.	exp Meta-Analysis as Topic/
57.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
58.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
59.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
60.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
61.	(search* adj4 literature).ab.
62.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
63.	cochrane.jw.
64.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
65.	or/55-64
66.	randomized controlled trial.pt.
67.	controlled clinical trial.pt.
68.	randomi#ed.ti,ab.
69.	placebo.ab.
70.	randomly.ti,ab.
71.	Clinical Trials as topic.sh.
72.	trial.ti.
73.	or/66-72
74.	28 and (39 or 54 or 65 or 73)
75.	hydrocephalus/ or hydrocephalus, normal pressure/

76.	(hydrocephalus or hydrocephaly).ti,ab.
77.	water on the brain.ti,ab.
78.	or/75-77
79.	74 and 78

Embase (Ovid) search terms

1.	*subarachnoid hemorrhage/
2.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) adj3 (hemorrhag* or haemorrhag* or bleed* or blood*)).ti,ab.
3.	(SAH or aSAH).ti,ab.
4.	exp intracranial aneurysm/
5.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial or brain or saccular or berry or wide-neck*) adj3 (aneurysm* or aneurism* or hematoma* or haematoma*)).ti,ab.
6.	or/1-5
7.	letter.pt. or letter/
8.	note.pt.
9.	editorial.pt.
10.	Case report/ or Case study/
11.	(letter or comment*).ti.
12.	or/7-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animal/ not human/
16.	Nonhuman/
17.	exp Animal Experiment/
18.	exp Experimental animal/
19.	Animal model/
20.	exp Rodent/
21.	(rat or rats or mouse or mice).ti.
22.	or/14-21
23.	6 not 22
24.	(exp child/ or exp pediatrics/) not (exp adult/ or exp adolescent/)
25.	23 not 24
26.	limit 25 to English language
27.	exp "sensitivity and specificity"/
28.	(sensitivity or specificity).ti,ab.
29.	((pre test or pretest or post test) adj probability).ti,ab.
30.	(predictive value* or PPV or NPV).ti,ab.
31.	likelihood ratio*.ti,ab.
32.	((area under adj4 curve) or AUC).ti,ab.
33.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
34.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
35.	diagnostic accuracy/
36.	diagnostic test accuracy study/
37.	gold standard.ab.

38.	or/27-37
39.	Clinical study/
40.	Observational study/
41.	family study/
42.	longitudinal study/
43.	retrospective study/
44.	prospective study/
45.	cohort analysis/
46.	follow-up/
47.	cohort*.ti,ab.
48.	46 and 47
49.	(cohort adj (study or studies or analys* or data)).ti,ab.
50.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
51.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
52.	(before adj2 after adj2 (study or studies or data)).ti,ab.
53.	exp case control study/
54.	case control*.ti,ab.
55.	cross-sectional study/
56.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
57.	or/39-45,48-56
58.	random*.ti,ab.
59.	factorial*.ti,ab.
60.	(crossover* or cross over*).ti,ab.
61.	((doubl* or singl*) adj blind*).ti,ab.
62.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
63.	crossover procedure/
64.	single blind procedure/
65.	randomized controlled trial/
66.	double blind procedure/
67.	or/58-66
68.	systematic review/
69.	meta-analysis/
70.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
71.	((systematic or evidence) adj3 (review* or overview*)).ti,ab.
72.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
73.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
74.	(search* adj4 literature).ab.
75.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
76.	cochrane.jw.
77.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
78.	or/68-77
79.	26 and (38 or 57 or 67 or 78)

80.	normotensive hydrocephalus/ or hydrocephalus/
81.	(hydrocephalus or hydrocephaly).ti,ab.
82.	water on the brain.ti,ab.
83.	or/80-82
84.	79 and 83

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Subarachnoid Hemorrhage] explode all trees
#2.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) near/3 (hemorrhag* or haemorrhag* or bleed* or blood*)):ti,ab
#3.	(SAH or aSAH):ti,ab
#4.	MeSH descriptor: [Intracranial Aneurysm] explode all trees
#5.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial or brain or saccular or berry or wide-neck*) near/3 (aneurysm* or aneurism* or hematoma* or haematoma*)):ti,ab
#6.	(OR #1-#5)
#7.	MeSH descriptor: [Hydrocephalus] explode all trees
#8.	(hydrocephalus or hydrocephaly):ti,ab
#9.	water on the brain.ti,ab
#10.	(or #7-#9)
#11.	#6 and #10

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to subarachnoid haemorrhage population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase.

Table 6: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2003 – 23 June 2020	Exclusions Health economics studies
Embase	2003 – 23 June 2020	Exclusions Health economics studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 23 June 2020 NHSEED - Inception to March 2015	None

Medline (Ovid) search terms

1.	exp Subarachnoid Hemorrhage/
2.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) adj3 (hemorrhag* or haemorrhag* or bleed* or blood*)).ti,ab.
3.	(SAH or aSAH).ti,ab.
4.	exp Intracranial Aneurysm/

5.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial or brain or saccular or berry or wide-neck*) adj3 (aneurysm* or aneurism* or hematoma* or haematoma*)).ti,ab.
6.	or/1-5
7.	letter/
8.	editorial/
9.	news/
10.	exp historical article/
11.	Anecdotes as Topic/
12.	comment/
13.	case report/
14.	(letter or comment*).ti.
15.	or/7-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animals/ not humans/
19.	exp Animals, Laboratory/
20.	exp Animal Experimentation/
21.	exp Models, Animal/
22.	exp Rodentia/
23.	(rat or rats or mouse or mice).ti.
24.	or/17-23
25.	6 not 24
26.	limit 25 to English language
27.	Economics/
28.	Value of life/
29.	exp "Costs and Cost Analysis"/
30.	exp Economics, Hospital/
31.	exp Economics, Medical/
32.	Economics, Nursing/
33.	Economics, Pharmaceutical/
34.	exp "Fees and Charges"/
35.	exp Budgets/
36.	budget*.ti,ab.
37.	cost*.ti.
38.	(economic* or pharmaco?economic*).ti.
39.	(price* or pricing*).ti,ab.
40.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
41.	(financ* or fee or fees).ti,ab.
42.	(value adj2 (money or monetary)).ti,ab.
43.	or/27-42
44.	26 and 43

Embase (Ovid) search terms

1.	subarachnoid hemorrhage/

2.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) adj3 (hemorrhag* or haemorrhag* or bleed* or blood*)).ti,ab.
3.	(SAH or aSAH).ti,ab.
4.	exp intracranial aneurysm/
5.	((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial or brain or saccular or berry or wide-neck*) adj3 (aneurysm* or aneurism* or hematoma* or haematoma*)).ti,ab.
6.	or/1-5
7.	letter.pt. or letter/
8.	note.pt.
9.	editorial.pt.
10.	case report/ or case study/
11.	(letter or comment*).ti.
12.	or/7-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animal/ not human/
16.	nonhuman/
17.	exp Animal Experiment/
18.	exp Experimental Animal/
19.	animal model/
20.	exp Rodent/
21.	(rat or rats or mouse or mice).ti.
22.	or/14-21
23.	6 not 22
24.	limit 23 to English language
25.	health economics/
26.	exp economic evaluation/
27.	exp health care cost/
28.	exp fee/
29.	budget/
30.	funding/
31.	budget*.ti,ab.
32.	cost*.ti.
33.	(economic* or pharmaco?economic*).ti.
34.	(price* or pricing*).ti,ab.
35.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
36.	(financ* or fee or fees).ti,ab.
37.	(value adj2 (money or monetary)).ti,ab.
38.	or/25-37
39.	24 and 38

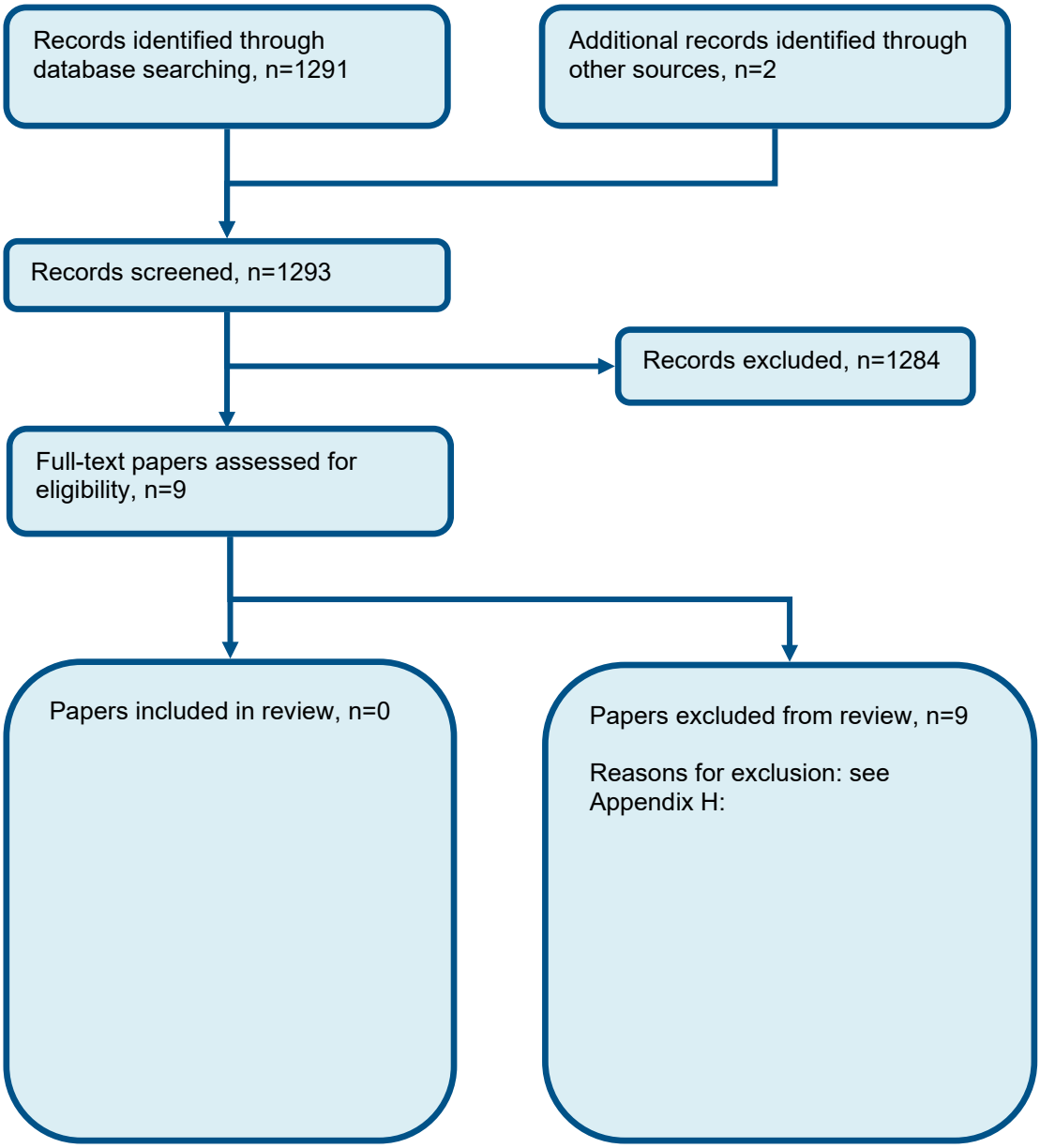
NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Subarachnoid Hemorrhage EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Intracranial Hemorrhages EXPLODE ALL TREES

#3.	(((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) adj3 (hemorrhag* or haemorrhag* or bleed* or blood*)))
#4.	((SAH or aSAH))
#5.	#1 OR #2 OR #3 OR #4
#6.	MeSH DESCRIPTOR Aneurysm EXPLODE ALL TREES
#7.	((aneurysm* or hematoma* or haematoma*))
#8.	#6 OR #7
#9.	MeSH DESCRIPTOR Intracranial Aneurysm EXPLODE ALL TREES
#10.	(((subarachnoid* or arachnoid* or cerebral or intracranial or intra-cranial) adj3 (aneurysm* or hematoma* or haematoma*)))
#11.	#9 OR #10
#12.	MeSH DESCRIPTOR Aneurysm, ruptured
#13.	(((ruptur* or weak* or brain or trauma*) adj3 (aneurysm* or hematoma* or haematoma*)))
#14.	#12 OR #13
#15.	(#5 or #8 or #11 or #14)

Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of detecting hydrocephalus



Appendix D: Clinical evidence tables

No evidence was identified for this review

Appendix E: Coupled sensitivity and specificity forest plots and sROC curves

E.1 Coupled sensitivity and specificity forest plots

No evidence was identified for this review.

E.2 ROC curves

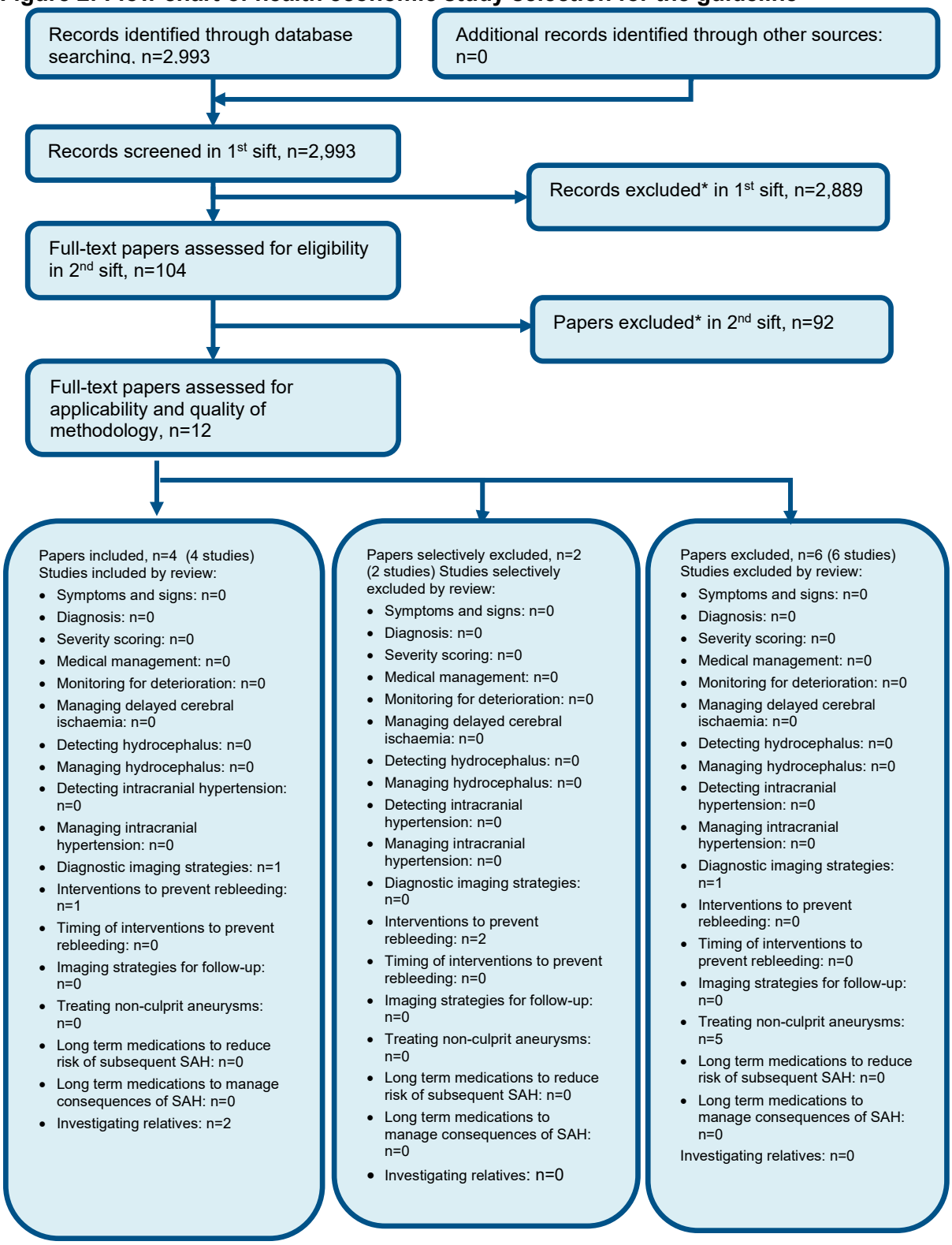
No evidence was identified for this review.

E.3 Area under the curve

No evidence was identified for this review.

Appendix F: Health economic evidence selection

Figure 2: Flow chart of health economic study selection for the guideline



* Non-relevant population, intervention, comparison, design or setting; non-English language

Appendix G: Health economic evidence tables

None.

Appendix H: Excluded studies

H.1 Excluded clinical studies

Table 7: Studies excluded from the clinical review

Reference	Reason for exclusion
Andaluz 2008[1]	Inappropriate study design – no relevant outcomes
Duong 1996[2]	Inappropriate study design – case series
Łuczywek 2000[3]	Paper not in English
Mortimer 2016[4]	Inappropriate study design – no relevant outcomes
Ohmichi 2018[7]	Inappropriate comparison – assessment of hyperperfusion
Pascual 2008[8]	Inappropriate population – headaches provoked by cough
Peschillo 2017[9]	Inappropriate comparison – flow diversion vs coiling
Stadlbauer 2012[10]	Inappropriate comparison – MR mapping
Woodfield 2014[11]	Inappropriate study design – unclear methodology

H.2 Excluded health economic studies

Published health economic studies that met the inclusion criteria (relevant population, comparators, economic study design, published 2003 or later and not from non-OECD country or USA) but that were excluded following appraisal of applicability and methodological quality are listed below. See the health economic protocol for more details.

Table 8: Studies excluded from the health economic review

Reference	Reason for exclusion
None.	